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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,703	LE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,7-10 and 14-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,7-10 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

INCLUDING PREVIOUS MAILED 892's PER APPLICANT'S REQUEST

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 5/26/05 has been entered.

Applicant's amendment, filed 5/26/05, has been entered.
Claims 1, 5 and 11-13 have been canceled. Claims 2 and 6 have been canceled previously.
Claims 3, 4, 7 and 8 have been amended.
Claims 14-19 have been added.

Claims 1, 3-5 and 7-13 are pending and being acted upon presently.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments, filed 5/26/05.
The rejections of record can be found in the previous Office Action.

3. With respect to the previous submitted IDSs, the examiner initialed the citations to Related Applications, indicating consideration of said applications, but crossed out the application itself, as being not appropriate for printing on the face of a U.S. Patent.

4. The filing date of the instant claims is still deemed to be the filing date of the priority application USSN 08/570,674, filed 12/11/95, as the previous priority applications do not support the claimed limitations of the instant application, encompassing methods of treating "psoriasis".

Again, applicant relies upon the disclosure of " treating diseases including chronic inflammatory diseases with anti-TNF antibodies" in the priority document USSN 07/680,827, filed 3/18/91 in conjunction with Exhibit A (Fauci et al. in Harrisons Principles of Internal Medicine 300, McGraw-Hill 14th Edition, 1998) indicating that psoriasis is a chronic inflammatory disease to support the priority of the instant claims back to USSN 07/680,827, filed 3/18/91.

However, the generic disclosure of treating chronic inflammatory diseases" does not provide sufficient written description for the recitation of the species "psoriasis", even if "psoriasis" was considered a chronic inflammatory condition at the time the invention was made.

Alternatively, applicant submits that if the PCT application WO 92/16553 is sufficient to qualify as prior art, then the instant application should be afforded the priority date of applicant's disclosure in the priority application USSN 07/853,606, filed 3!8/92.

Applicant is reminded that: A claim as a whole has only one effective filing date.
See Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

While applicant attempts to distinguish the holdings of Ex parte Batchelder, 131 USPQ 38, 39 (1960). and Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) from the instant efforts to claim an earlier priority date,

Applicant's claims drawn to treating "psoriasis" involves introducing elements or limitations where were not supported by the as-filed disclosures of the earliest priority documents, asserted by applicant.

The following of record is noted again for applicant's convenience.

Limitation of a class, generically disclosed, to a subgenus without any teaching of the subgenus is new matter unsupported by the specification. Ex parte Batchelder, 131 USPQ 38, 39 (1960).

It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Applicant's arguments are not found persuasive and the filing date of the instant claims is still deemed to be the filing date of the priority application USSN 08/570,674, filed 12/11/95.

5. Applicant's amendment reiterates the fact that that the biological materials for cA2 have not been publicly deposited.

Again, this appears to be inconsistent with the patented claims set forth in U.S. Patent No. 5,698,195 (Le et al.), wherein it is believed that the requirement for the deposit of the biological materials cA2 antibodies under 35 USC § 112, first paragraph, enablement, had been satisfied.

As noted previously and in contrast to applicant's assertions and reliance upon the disclosure of the instant specification and In re Wands 8 USPQ2d 1400 (Fed. Cir. 1988), it is apparent that the cA2 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

Again, it is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin.

Note that satisfaction for the biological deposit of the specific cA2 antibody requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences.

Therefore, in order to satisfy the enablement requirements under U.S.C. § 112, first paragraph, with respect to the cA2 antibody with respect to claims 3, 4, and 14-19, either satisfying the deposit of the appropriate cell line that produces the cA2 antibody or providing the sequence of the entire immunoglobulin is required.

Applicant's arguments in conjunction with the prosecution history of U.S. Patents Nos. 5,698,195, 5919,452 and 6,790,444, the Vilcek Declaration have been fully considered but are not found convincing essentially for the reasons of record.

It unclear if a cell line which produces an antibody having the exact structural and chemical identity of cA2 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species cA2. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

However, biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question from a source prior to and after the filing date of the application does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public.

There is no assurance that a depository would allow unlimited access to the material if the application has matured into a patent. In the absence of evidence that the cA2 antibody / hybridoma / cell line is readily available to the public and that all restrictions imposed by a recognized depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, applicant's arguments are not persuasive and the rejection is maintained.

Further, it is noted that it is unclear if a cell line which has the exact structural and chemical identity of the cA2 antibody can be reproducibly isolated without undue experimentation. Replication of the claimed cell line an unpredictable event. Further, a particular biological cell line can undergo changes resulting in microheterogeneity. Therefore, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed.

If applicant amends the claims to rely upon the cA2 antibody defined by the specific light chain variable region of SEQ ID NO: 3, the heavy chain region of SEQ ID NO: 5 and the human constant region of IgG1 kappa as disclosed in the instant specification as filed,
then the instant rejection may be obviated.

See the Reasons for Allowance in U.S. Patent No. 6,790,444, filed as USSN 09/756,301.

Applicant's arguments are not found persuasive.

6. Claims 3, 4 and 14-19 are rejected under 35 U.S.C. ∋ 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 4 and 14-19 are indefinite in the recitation of "cA2" antibody because its characteristics are not known. The use of "cA2" antibody as the sole means of identifying the claimed antibody renders the claims indefinite because this designation is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct cell lines.

Amending the claims to recite the appropriate ATCC Accession Numbers or the appropriate SEQ ID NOS. of the entire cA2 antibody would obviate this rejection.

Given the number of patents from the priority documents, applicant is invited to make a positive statement that the claimed cA2 antibody is the same cA2 antibody deposited by the appropriate ATCC Accession Numbers or set forth in the appropriate SEQ ID NOS. of the entire cA2 antibody would obviate this rejection.

If the intent of the recitation of cA2 is not a specific antibody but reflects a TNF specificity, then applicant is required to amend the claims to recite an ATCC Accession Number or the appropriate SEQ ID NOS. that define the cA2 to obviate this rejection.

Applicant's arguments, filed 5/26/05, have been fully considered but are not found convincing essentially for the reasons of record.

Given the ambiguity indicated above concerning satisfying the enablement requirements for the biological materials such as the cA2 antibody in U.S. Patents addressed above, this rejection is maintained.

Again, applicant's reliance on published articles does not satisfy the requirement that cA2 particularly points out and distinctly claims the particular anti-TNF cA2 antibody asserted by applicant.
Applicant is on record that the cA2 antibody has not been deposited.

Applicant should specifically point out the support for any amendments made to the disclosure.
See MPEP 714.02 and 2163.06

7. The previous rejection under 35 USC 102(e) as being anticipated by Adair et al. (U.S. Patent No. 5,994,510) has been obviated by applicant's canceled claims.

8. Claims 3, 4, 7-10 and 14-19 are rejected under 35 U.S.C.§ 103(a) as being unpatentable over Adair et al. (U.S. Patent No. 5,994,510) in view of Le et al. (WO 92/16553) for the reasons of record.

Applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

A prior art reference may be considered to teach away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." See In re Gurley , 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Here in contrast to applicant's assertions of teaching away by the prior art because the references indicate advantages of humanized antibodies over chimeric antibodies particularly for treatment over prolonged periods of time to avoid immune responses; there is no statement that the ordinary artisan should not or could not treati patients with chimeric antibodies per se at the time the invention was made.

Although applicant asserts unexpected results, the prior art teaches the use of anti-TNF antibodies, including the cA2 anti-TNF antibody to treat a number of conditions. Therefore, there was an expectation of success in treating patients with various inflammatory or autoimmune conditions at the time the invention was made.

Again as indicated above, applicant's reliance upon the priority date of priority application USSN 07/670,827, filed 3/18/91, has not been found convincing with respect to the treatment of psoriasis with anti-TNF antibodies that compete with cA2.

Therefore, the rejection of record is maintained for the reasons of record and reiterated herein for applicant's convenience.

Adair et al. teach methods of inhibiting patients suffering disorders associated with undesirably high levels of TNF, including psoriasis (e.g. see columns 1-12, including column 11, line 52) with TNFα-specific antibodies, including recombinant chimeric and humanized antibodies (see Detailed Description of the Invention) (see entire document).

Adair et al. differs from the claimed methods by not disclosing Aanti-TNF antibody competitively inhibits binding of TNF to monoclonal antibody cA2" or "anti-TNF antibody binds to at least one epitope included in amino acids between 87-108 or both 59-80 or 87-108 of SEQ ID NO: 1 of hTNF" as the anti-TNFα antibody specificities employed in the claimed methods.

Le et al. (WO 92/16553) teach methods of treating autoimmune disorders with anti-TNFα antibody, including the cA2 anti-TNFα antibody specificity and including its epitopic specificity (e.g. pages 9-10, overlapping paragraph; page 13, paragraph 1; page 15, page 20; page 22) (see entire document, including Summary of the Invention, Detailed Description of the Preferred Embodiments and Examples).

Given the inhibitory properties of the cA2 TNFα-specific antibodies taught by Le et al., one of ordinary skill in the art at the time the invention was made would have been motivated to substitute the cA2 anti-TNFα antibody specificity into the methods of treating psoriasis with TNFα-specific antibodies taught by Adair et al. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Given the well known use of therapeutic antibodies that have decreased immunogenicity to overcome neutralizing effects of the immune response in human patients, it had been well accepted practice by the ordinary skill in the art at the time the invention was made to employ therapeutic antibodies will decreased immunogenicity, such as chimeric antibodies, humanized antibodies, as taught above as well as human antibodies. One of ordinary skill in the art human antibodies, one of ordinary skill in the art at the time the invention was made would have been motivated to modify the anti-TNFα antibodies or the cA2-specific anti-TNFα antibodies by making them human to decrease immunogenicity in the methods of treating psoriasis with TNFα-specific antibodies taught by Adair et al. The newly added limitations of dosing and administration, including the use of combination therapy were well within the purview of the ordinary artisan to meet the needs of the patient as well as being consistent with such dosing and combination therapies taught by the prior art references (e.g. see columns 11-12 of Adair et al. and pages 34-38 of Le et al.) From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. No claim allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 572-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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August 22, 2005